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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
 NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
 NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
 NEWS 4 Apr 09 ZDB will be removed from STN
 NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
 NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
 NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
 NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
 NEWS 9 Jun 03 New e-mail delivery for search results now available
 NEWS 10 Jun 10 MEDLINE Reload
 NEWS 11 Jun 10 PCTFULL has been reloaded
 NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
 NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
 saved answer sets no longer valid
 NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
 NEWS 15 Jul 30 NETFIRST to be removed from STN
 NEWS 16 Aug 08 CANCERLIT reload
 NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
 NEWS 18 Aug 08 NTIS has been reloaded and enhanced
 NEWS 19 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
 now available on STN
 NEWS 20 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
 NEWS 21 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded
 NEWS 22 Aug 26 Sequence searching in REGISTRY enhanced
 NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
 NEWS 24 Sep 16 Experimental properties added to the REGISTRY file
 NEWS 25 Sep 16 CA Section Thesaurus available in CAPLUS and CA
 NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 27 Oct 21 EVENTLINE has been reloaded
 NEWS 28 Oct 24 BEILSTEIN adds new search fields
 NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
 NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
 NEWS 31 Nov 18 DKILIT has been renamed APOLLIT
 NEWS 32 Nov 25 More calculated properties added to REGISTRY
 NEWS 33 Dec 02 TIBKAT will be removed from STN
 NEWS 34 Dec 04 CSA files on STN
 NEWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
 NEWS 36 Dec 17 TOXCENTER enhanced with additional content
 NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
 NEWS 38 Dec 30 ISMEC no longer available
 NEWS 39 Jan 13 Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003
 NEWS 41 Jan 21 PHARMAML offering one free connect hour in February 2003
 NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
 ENERGY, INSPEC

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
 CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
 AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002

NEWS HOURS STN Operating Hours Plus Help Desk Availability

NEWS INTER General Internet Information
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 NEWS WWW CAS World Wide Web Site (general information)

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 12:13:36 ON 03 FEB 2003

=> fil reg

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 12:13:55 ON 03 FEB 2003

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STRUCTURE FILE UPDATES: 2 FEB 2003 HIGHEST RN 484639-64-7

DICTIONARY FILE UPDATES: 2 FEB 2003 HIGHEST RN 484639-64-7

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNnote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> e monoterpene?

| | | |
|-----|-------|-------------------|
| E1 | 30 | MONOTERPEN/BI |
| E2 | 25 | MONOTERPENE/BI |
| E3 | 0 --> | MONOTERPENE?/BI |
| E4 | 1 | MONOTERPENES/BI |
| E5 | 1 | MONOTERPENOID/BI |
| E6 | 7 | MONOTERPENOL/BI |
| E7 | 1 | MONOTERPENOLS/BI |
| E8 | 1 | MONOTERPENYL/BI |
| E9 | 2 | MONOTES/BI |
| E10 | 2 | MONOTESONE/BI |
| E11 | 53 | MONOTETRA/BI |
| E12 | 2 | MONOTETRABROMO/BI |

=> s e1 or e2 or r4

30 MONOTERPEN/BI
25 MONOTERPENE/BI
148 R4

L1 178 MONOTERPEN/BI OR MONOTERPENE/BI OR R4

=> e monoterpene

E1 2 MONOTEREPHTHALOYLHYDRAZONE/BI
E2 30 MONOTERPEN/BI
E3 25 --> MONOTERPENE/BI
E4 1 MONOTERPENES/BI
E5 1 MONOTERPENOID/BI
E6 7 MONOTERPENOL/BI
E7 1 MONOTERPENOLS/BI
E8 1 MONOTERPENYL/BI
E9 2 MONOTES/BI
E10 2 MONOTESONE/BI
E11 53 MONOTETRA/BI
E12 2 MONOTETRABROMO/BI

=> s e2 or e3 or e4

30 MONOTERPEN/BI
25 MONOTERPENE/BI
1 MONOTERPENES/BI

L2 30 MONOTERPEN/BI OR MONOTERPENE/BI OR MONOTERPENES/BI

=> e sesquiterpene?

E1 52 SESQUITERPEN/BI
E2 48 SESQUITERPENE/BI
E3 0 --> SESQUITERPENE?/BI
E4 4 SESQUITERPENES/BI
E5 2 SESQUITERPENOID/BI
E6 1 SESQUITERPENOIDAL/BI
E7 4 SESQUITERPENIDS/BI
E8 1 SESQUITERPENOL/BI
E9 1 SESQUITERPINE/BI
E10 1 SESQUITERPINEN/BI
E11 1 SESQUITERPINENOL/BI
E12 1 SESQUITETRA/BI

=> s e1 or e2 or e4

52 SESQUITERPEN/BI
48 SESQUITERPENE/BI
4 SESQUITERPENES/BI

L3 52 SESQUITERPEN/BI OR SESQUITERPENE/BI OR SESQUITERPENES/BI

=> fil .search

COST IN U.S. DOLLARS

| SINCE FILE | TOTAL |
|------------|---------|
| ENTRY | SESSION |
| 39.58 | 39.79 |

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 12:16:30 ON 03 FEB 2003

FILE 'CAPLUS' ENTERED AT 12:16:30 ON 03 FEB 2003

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FILE 'BIOSIS' ENTERED AT 12:16:30 ON 03 FEB 2003

COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

FILE 'USPATFULL' ENTERED AT 12:16:30 ON 03 FEB 2003

CA INDEXING COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 12:16:30 ON 03 FEB 2003
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=> d his

(FILE 'HOME' ENTERED AT 12:13:36 ON 03 FEB 2003)

FILE 'REGISTRY' ENTERED AT 12:13:55 ON 03 FEB 2003

 E MONOTERPENE?
L1 178 S E1 OR E2 OR R4
 E MONOTERPENE
L2 30 S E2 OR E3 OR E4
 E SESQUITERPENE?
L3 52 S E1 OR E2 OR E4

FILE 'MEDLINE, CAPLUS, BIOSIS, USPATFULL, EMBASE' ENTERED AT 12:16:30 ON
03 FEB 2003

=> s l2 or l3

L4 1412 L2 OR L3

=> s l4 and (tumor? or tumour?)

L5 20 L4 AND (TUMOR? OR TUMOUR?)

=> dup rem l5

PROCESSING COMPLETED FOR L5

L6 18 DUP REM L5 (2 DUPLICATES REMOVED)

=> d ibib ab 1-

YOU HAVE REQUESTED DATA FROM 18 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 18 USPATFULL
 ACCESSION NUMBER: 2002:67348 USPATFULL
 TITLE: Sesquiterpene synthases from grand fir (*Abies grandis*),
 and methods of use
 INVENTOR(S): Croteau, Rodney Bruce, Pullman, WA, UNITED STATES
 Bohlmann, Jorg, Jens, GERMANY, FEDERAL REPUBLIC OF
 Crock, John E., Moscow, ID, UNITED STATES
 Steele, Christopher L., Admore, OK, UNITED STATES
 PATENT ASSIGNEE(S): Washington State University Research Foundation (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 2002038001 | A1 | 20020328 |
| | US 6451576 | B2 | 20020917 |
| APPLICATION INFO.: | US 2001-865171 | A1 | 20010524 (9) |
| RELATED APPLN. INFO.: | Division of Ser. No. US 1999-234393, filed on 20 Jan 1999, GRANTED, Pat. No. US 6265639 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1998-72204P | 19980122 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC, 1420 FIFTH AVENUE, SUITE 2800, SEATTLE, WA, 98101-2347 | |
| NUMBER OF CLAIMS: | 29 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 4 Drawing Page(s) | |
| LINE COUNT: | 5307 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB cDNAs encoding E-.alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase from Grand Fir (*Abies grandis*) have been isolated and sequenced, and the corresponding amino acid sequences have been determined. Accordingly, isolated DNA sequences (SEQ ID No:12; SEQ ID No:19 and SEQ ID No:23) are provided which code for the expression of E-.alpha.-bisabolene synthase (SEQ ID No:13), .delta.-selinene synthase (SEQ ID No:20) and .gamma.-humulene synthase (SEQ ID No:24), respectively, from Grand Fir (*Abies grandis*). In other aspects, replicable recombinant cloning vehicles are provided which code for E-.alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase, or for a base sequence sufficiently complementary to at least a portion of E-.alpha.-bisabolene synthase, .delta.-selinene synthase or .gamma.-humulene synthase DNA or RNA to enable hybridization therewith. In yet other aspects, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding E-.alpha.-bisabolene synthase, .delta.-selinene synthase or .gamma.-humulene synthase. Thus, systems and methods are provided for the recombinant expression of the aforementioned recombinant sesquiterpene synthases that may be used to facilitate their production, isolation and purification in significant amounts. Recombinant

L6 ANSWER 2 OF 18 USPATFULL
 ACCESSION NUMBER: 2002:194743 USPATFULL
 TITLE: Monoterpene synthases from grand fir (*Abies grandis*)
 INVENTOR(S): Steele, C. L., Ardmore, OK, United States
 Bohlmann, Joerg, Jens, GERMANY, FEDERAL REPUBLIC OF
 Croteau, Rodney B., Pullman, WA, United States
 PATENT ASSIGNEE(S): Washington State University Research Foundation, Pullman, WA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6429014 | B1 | 20020806 |
| APPLICATION INFO.: | US 1999-360545 | | 19990726 (9) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. WO 1998-US14528, filed on 10 Jul 1998 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1997-52249P | 19970711 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Bui, Phuong T. | |
| LEGAL REPRESENTATIVE: | Christensen O'Connor Johnson Kindness PLLC | |
| NUMBER OF CLAIMS: | 12 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 25 Drawing Figure(s); 25 Drawing Page(s) | |
| LINE COUNT: | 5595 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB cDNAs encoding gymnosperm monoterpene synthases have been isolated and sequenced, and the corresponding amino acid sequences have been determined. Modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding a monoterpene synthase of the invention. Thus, systems and methods are provided for the recombinant expression of recombinant monoterpene synthases that may be used to facilitate their production, isolation and purification in significant amounts.

L6 ANSWER 1 OF 18 USPATFULL (Continued)

E-.alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase may be used to obtain expression or enhanced expression of E-.alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase in plants in order to enhance the production of sesquiterpenoids, or may be otherwise employed for the regulation or expression of E-.alpha.-bisabolene synthase, .delta.-selinene synthase and .gamma.-humulene synthase, or the production of their products.

L6 ANSWER 3 OF 18 USPATFULL
 ACCESSION NUMBER: 2001:178834 USPATFULL
 TITLE: Geranyl diphosphate synthase large subunit, and methods
 INVENTOR(S): Croteau, Rodney B., Pullman, WA, United States
 Burke, Charles C., Moscow, ID, United States
 Wildung, Mark R., Colfax, WA, United States
 PATENT ASSIGNEE(S): Washington State University Research Foundation, Pullman, WA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 6303330 | B1 | 20011016 |
| APPLICATION INFO.: | US 1999-420211 | | 19991018 (9) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. WO 1998-US21772, filed on 15 Oct 1998 Continuation-in-part of Ser. No. US 1997-951924, filed on 16 Oct 1997, now patented, Pat. No. US 5876964 | | |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1997-52249P | 19970711 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Brusca, John S. | |
| LEGAL REPRESENTATIVE: | Christensen O'Connor Johnson Kindness PLLC | |
| NUMBER OF CLAIMS: | 24 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 2 Drawing Figure(s); 2 Drawing Page(s) | |
| LINE COUNT: | 2145 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A cDNA encoding geranyl diphosphate synthase large subunit from peppermint has been isolated and sequenced, and the corresponding amino acid sequence has been determined. Replicable recombinant cloning vehicles are provided which code for geranyl diphosphate synthase large subunit. In another aspect, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding geranyl diphosphate synthase large subunit. In yet another aspect, the present invention provides isolated, recombinant geranyl diphosphate synthase protein comprising an isolated, recombinant geranyl diphosphate synthase large subunit protein and an isolated, recombinant geranyl diphosphate synthase small subunit protein. Thus, systems and methods are provided for the recombinant expression of geranyl diphosphate synthase.

L6 ANSWER 4 OF 18 USPATFULL
 ACCESSION NUMBER: 2001:117244 USPATFULL
 TITLE: Gymnosperm nucleic acid molecules encoding sesquiterpene synthases and methods of use
 INVENTOR(S): Croteau, Rodney Bruce, Pullman, WA, United States
 Bohlmann, Jorg, Jena, Germany, Federal Republic of
 Jetter, Reinhard, Wurzburg, Germany, Federal Republic of
 Crock, John E., Moscow, ID, United States
 Steele, Christopher L., Admore, OK, United States
 PATENT ASSIGNEE(S): Washington State University Foundation, Pullman, WA, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 6265639 | B1 | 20010724 |
| APPLICATION INFO.: | US 1999-234393 | | 19990120 (9) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 1998-72204P | 19980123 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | GRANTED | |
| PRIMARY EXAMINER: | Nelson, Amy J. | |
| LEGAL REPRESENTATIVE: | Christensen O'Connor Johnson Kindness PLLC | |
| NUMBER OF CLAIMS: | 17 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 4 Drawing Figure(s); 4 Drawing Page(s) | |
| LINE COUNT: | 2543 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB cDNAs encoding E-.alpha.-bisabolene synthase, .delta.-seline synthase and .gamma.-humulene synthase from Grand Fir (*Abies grandis*) have been isolated and sequenced, and the corresponding amino acid sequences have been determined. Accordingly, isolated DNA sequences (SEQ ID No:12 and SEQ ID No:19 and SEQ ID No:23) are provided which code for the expression of E-.alpha.-bisabolene synthase (SEQ ID No:13), .delta.-seline synthase (SEQ ID No:20) and .gamma.-humulene synthase (SEQ ID No: 24), respectively, from Grand Fir (*Abies grandis*). In other aspects, replicable recombinant cloning vehicles are provided which

code for E-.alpha.-bisabolene synthase, .delta.-seline synthase and .gamma.-humulene synthase, or for a base sequence sufficiently complementary to at least a portion of E-.alpha.-bisabolene synthase, .delta.-seline synthase or .gamma.-humulene synthase DNA or RNA to enable hybridization therewith. In yet other aspects, modified host cells are provided that have been transformed, transfected, infected and/or injected with a recombinant cloning vehicle and/or DNA sequence encoding E-.alpha.-bisabolene synthase, .delta.-seline synthase or .gamma.-humulene synthase. Thus, systems and methods are provided for the recombinant expression of the aforementioned recombinant sesquiterpene synthases that may be used to facilitate their production, isolation and purification in significant amounts. Recombinant E-.alpha.-bisabolene synthase, .delta.-seline synthase and .gamma.-humulene synthase may be used to obtain expression or enhanced expression of E-.alpha.-bisabolene synthase, .delta.-seline synthase and .gamma.-humulene synthase in plants, or may be otherwise employed

L6 ANSWER 5 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 2001:567520 BIOSIS
 DOCUMENT NUMBER: PREV200100567520
 TITLE: The GDNF/RET signaling pathway and human diseases.
 AUTHOR(S): Takahashi, Masahide (1)
 CORPORATE SOURCE: (1) Department of Pathology, Graduate School of Medicine, Nagoya University, 65 Tsurumai-cho, Showa-ku, Nagoya, 466-8550; mtakaha@med.nagoya-u.ac.jp Japan
 SOURCE: Cytokine & Growth Factor Reviews, (December, 2001) Vol. 12, No. 4, pp. 361-373. print.
 ISSN: 1359-6101.
 DOCUMENT TYPE: General Review
 LANGUAGE: English
 SUMMARY LANGUAGE: English

L6 ANSWER 4 OF 18 USPATFULL (Continued)
 for the regulation or expression of E-.alpha.-bisabolene synthase, .delta.-seline synthase and .gamma.-humulene synthase.

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6072045 | | 20000606 |
| APPLICATION INFO.: | US 1998-134699 | | 19980814 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1996-631341, filed on 12 Apr 1996, now patented, Pat. No. US 5824774 | | |

| | NUMBER | DATE |
|-----------------------|--|--------------|
| PATENT INFORMATION: | US 6072045 | 20000606 |
| APPLICATION INFO.: | US 1998-134699 | 19980814 (9) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1996-631341, filed on 12 Apr 1996, now patented, Pat. No. US 5824774 | |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | Granted | |
| PRIMARY EXAMINER: | Huff, Sheela | |
| LEGAL REPRESENTATIVE: | Clark & Elbing, LLP | |
| NUMBER OF CLAIMS: | 10 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 9 Drawing Figure(s); 9 Drawing Page(s) | |
| LINE COUNT: | 1337 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed is a chimeric isoprenoid synthase polypeptide including a first domain from a first isoprenoid synthase joined to a second domain from a second, heterologous isoprenoid synthase, whereby the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid reaction products that are not produced in the absence of the second domain of the second, heterologous isoprenoid synthase. Also disclosed is a chimeric isoprenoid synthase polypeptide including an asymmetrically positioned homologous domain, whereby the chimeric isoprenoid synthase is capable of catalyzing the production of isoprenoid reaction products that are not produced when the domain is positioned at its naturally-occurring site in the isoprenoid synthase polypeptide.

L6 ANSWER 7 OF 18 USPATFULL
 ACCESSION NUMBER: 1999:43445 USPATFULL
 TITLE: Monoterpene synthases from common sage (*Salvia officinalis*)
 INVENTOR(S): Croteau, Rodney Bruce, Pullman, WA, United States
 Wise, Mitchell Lynn, Pullman, WA, United States
 Katahira, Eva Joy, Pullman, WA, United States
 Savage, Thomas Jonathan, Christchurch 5, New Zealand
 PATENT ASSIGNEE(S): Washington State University Research Foundation,
 United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 5891697 | | 19990406 |
| APPLICATION INFO.: | US 1997-937540 | | 19970925 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Wax, Robert A. | | |
| ASSISTANT EXAMINER: | Saidha, Tekchand | | |
| LEGAL REPRESENTATIVE: | Christensen O'Connor Johnson & Kindness PLLC | | |
| NUMBER OF CLAIMS: | 20 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 1 Drawing Figure(s); 1 Drawing Page(s) | | |
| LINE COUNT: | 2204 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB cDNAs encoding (+)-bornyl diphosphate synthase, 1,8-cineole synthase
 and (+)-sabinene synthase from common sage (*Salvia officinalis*) have been
 isolated and sequenced, and the corresponding amino acid sequences has
 been determined. Accordingly, isolated DNA sequences (SEQ ID No:1; SEQ
 ID No:3 and SEQ ID No:5) are provided which code for the expression of
 (+)-bornyl diphosphate synthase (SEQ ID No:2), 1,8-cineole synthase
 (SEQ ID No:4) and (+)-sabinene synthase (SEQ ID No:6), respectively, from
 sage (*Salvia officinalis*). In other aspects, replicable recombinant cloning
 vehicles are provided which code for (+)-bornyl diphosphate synthase,
 1,8-cineole synthase or (+)-sabinene synthase, or for a base sequence
 sufficiently complementary to at least a portion of (+)-bornyl
 diphosphate synthase, 1,8-cineole synthase or (+)-sabinene synthase DNA
 or RNA to enable hybridization therewith. In yet other aspects,
 modified host cells are provided that have been transformed, transfected,
 infected and/or injected with a recombinant cloning vehicle and/or DNA
 sequence encoding (+)-bornyl diphosphate synthase, 1,8-cineole synthase
 or (+)-sabinene synthase. Thus, systems and methods are provided for
 the recombinant expression of the aforementioned recombinant monoterpene
 synthases that may be used to facilitate their production, isolation
 and purification in significant amounts. Recombinant (+)-bornyl diphosphate
 synthase, 1,8-cineole synthase and (+)-sabinene synthase may be used to
 obtain expression or enhanced expression of (+)-bornyl diphosphate
 synthase, 1,8-cineole synthase and (+)-sabinene synthase in plants in
 order to enhance the production of monoterpenoids, or may be otherwise
 employed for the regulation or expression of (+)-bornyl diphosphate

L6 ANSWER 7 OF 18 USPATFULL (Continued)
 synthase, 1,8-cineole synthase and (+)-sabinene synthase, or the
 production of their products.

L6 ANSWER 8 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 2000:61921 BIOSIS
 DOCUMENT NUMBER: PREV200000061921
 TITLE: Molecular mechanisms of RET activation in human
 neoplasia.
 AUTHOR(S): Santoro, M. (1); Carlomagno, F.; Melillo, R. M.; Billaud,
 M.; Vecchio, G.; Fusco, A.
 CORPORATE SOURCE: (1) Centro di Endocrinologia ed Oncologia Sperimentale del
 C.N.R., Universita degli Studi di Napoli, Via S. Pansini 5,
 80131, Napoli Italy
 SOURCE: Journal of Endocrinological Investigation, (Nov., 1999)
 Vol. 22, No. 10, pp. 811-819.
 ISSN: 0391-4097.
 DOCUMENT TYPE: General Review
 LANGUAGE: English

L6 ANSWER 9 OF 18 USPATFULL
 ACCESSION NUMBER: 1998:128159 USPATFULL
 TITLE: Chimeric isoprenoid synthases and uses thereof
 INVENTOR(S): Chappell, Joseph, Lexington, KY, United States
 Back, Kyoungwhan, Lexington, KY, United States
 PATENT ASSIGNEE(S): Board of Trustees of the University of Kentucky,
 Lexington, KY, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 5824774 | | 19981020 |
| APPLICATION INFO.: | US 1996-631341 | | 19960412 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Huff, Sheela | | |
| LEGAL REPRESENTATIVE: | Clark & Elbing LLP | | |
| NUMBER OF CLAIMS: | 18 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 9 Drawing Figure(s); 9 Drawing Page(s) | | |
| LINE COUNT: | 1388 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Disclosed is a chimeric isoprenoid synthase polypeptide including a
 first domain from a first isoprenoid synthase joined to a second domain
 from a second, heterologous isoprenoid synthase, whereby the chimeric
 isoprenoid synthase is capable of catalyzing the production of
 isoprenoid reaction products that are not produced in the absence of
 the second domain of the second, heterologous isoprenoid synthase. Also
 disclosed is a chimeric isoprenoid synthase polypeptide including an
 asymmetrically positioned homologous domain, whereby the chimeric
 isoprenoid synthase is capable of catalyzing the production of
 isoprenoid reaction products that are not produced when the domain is
 positioned at its naturally-occurring site in the isoprenoid synthase
 polypeptide.

L6 ANSWER 10 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1996:232423 BIOSIS
 DOCUMENT NUMBER: PREV199698796552
 TITLE: A cDNA clone for taxadiene synthase, the diterpene cyclase that catalyzes the committed step of taxol biosynthesis.
 AUTHOR(S): Wildung, Mark R.; Croteau, Rodney (1)
 CORPORATE SOURCE: (1) Inst. Biol. Chem., Washington State University, Pullman, WA 99164-6340 USA
 SOURCE: Journal of Biological Chemistry, (1996) Vol. 271, No. 16, pp. 9201-9204.
 ISSN: 0021-9258.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 AB The committed step of taxol (paclitaxel) biosynthesis is catalyzed by tax-4(5),11(12)-diene synthase, a diterpene cyclase responsible for transforming the ubiquitous isoprenoid intermediate geranylgeranyl diphosphate to the parent olefin with a taxane skeleton. To obtain the corresponding cDNA clone, a set of degenerate primers was constructed based on consensus sequences of related monoterpene, sesquiterpene, and diterpene cyclases. Two of these primers amplified 83-base pair fragment that was cyclase-like in sequence and that was employed as a hybridization probe to screen a cDNA library constructed from poly(A)+ RNA extracted from Pacific yew (*Taxus brevifolia*) stems. Twelve independent clones with insert size in excess of 2 kilobase pairs were isolated and partially sequenced. One of these cDNA isolates was functionally expressed in *Escherichia coli*, yielding a protein that was catalytically active in converting geranylgeranyl diphosphate to a diterpene olefin that was confirmed to be tax-4(5),11(12)-diene by combined capillary gas chromatography-mass spectrometry. The sequence specifies an open reading frame of 2586 nucleotides, and the complete deduced polypeptide, including a long presumptive plastidial targeting peptide, contains 862 amino acid residues and has a molecular weight of 98,303, compared with about 79,000 previously determined for the mature native enzyme. Sequence comparisons with monoterpene, sesquiterpene, and diterpene cyclases of plant origin indicate a significant degree of similarity between these enzymes; the taxadiene synthase most closely resembles (46% identity, 67% similarity) abietadiene synthase, a diterpene cyclase from grand fir.

L6 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1
 ACCESSION NUMBER: 1991:600896 CAPLUS
 DOCUMENT NUMBER: 115:200896
 TITLE: Carcinogenic activity of the pesticide olgin in a chronic experiment in rats
 AUTHOR(S): Petrovskaya, O. G.; Baglei, E. A.; Reehavekaya, E. V.
 CORPORATE SOURCE: All-Union Sci. Res. Inst. Hyg. Toxicol. Pestic., Polym. Plast., Kiev, 252127, USSR
 SOURCE: Eksperimental'naya Onkologiya (1991), 13(4), 18-20
 CODEN: EKSODD; ISSN: 0204-3564
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 AB Olgin administered orally to rats at doses of 0.30 and 30 mg/kg body wt. daily for 24 mo. promoted an increase in the tumor rate, the multiplicity index, and the relative risk and a decrease in the latent period. Tumor formation was high in the mammary gland, endocrine organs, and hemogenic tissues. No significant sex differences were found. The results demonstrated that olgin is carcinogenic.

L6 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1996:393156 CAPLUS
 DOCUMENT NUMBER: 125:52091
 TITLE: Identifying functional domains within terpene cyclases
 AUTHOR(S): Back, Kyoungwhan; Chappell, Joseph
 CORPORATE SOURCE: Plant Physiology/Biochemistry/Molecular Biology Program, University Kentucky, Lexington, KY, 40546-0091, USA
 SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(13), 6841-6845
 CODEN: PNASAG; ISSN: 0027-8424
 PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Cyclic terpenes and terpenoids are found throughout nature. They comprise an esp. important class of compds. from plants that mediate plant-environment interactions, and they serve as pharmaceutical agents with antimicrobial and anti-tumor activities. Mol. comparisons of several terpene cyclases, the key enzymes responsible for the multistep cyclization of C10, C15, and C20 allylic diphosphate substrates, have revealed a striking level of sequence similarity and conservation of exon position and size within the genes. Functional domains responsible for a terminal enzymic step were identified by swapping regions approximating exons between a *Nicotiana tabacum* 5-epiaristolochene synthase (TEAS) gene and a *Hyoscyamus muticus* vetispiradiene synthase (HVS) gene and by characterization of the resulting chimeric enzymes expressed in bacteria. While exon 4 of the TEAS gene conferred specificity for the predominant reaction products of the tobacco enzyme, exon 6 of the HVS gene conferred specificity for the predominant reaction product(s) of the *Hyoscyamus* enzyme. Combining these two functional domains of the TEAS and HVS genes resulted in a novel enzyme capable of synthesizing reaction products reflective of both parent enzymes. The relative ratio of the TEAS and HVS reaction products was also influenced by the source of exon 5 present in the new chimeric enzymes. The assocn. of catalytic activities with conserved but sep. exonic domains suggests a general means for generating addnl. novel terpene cyclases.

L6 ANSWER 13 OF 18 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
 ACCESSION NUMBER: 1989:319805 BIOSIS
 DOCUMENT NUMBER: BR37:22577
 TITLE: ELABORATION OF FUSED GEM-DIMETHYLCYCLOPROPANE SYSTEMS VIA CYCLOPROPENE CYCLOADDITION A STEREOCOMPLEMENTARY
 APPROACH:
 AUTHOR(S): RIGBY J H; KIERKUS P C
 CORPORATE SOURCE: DEP. CHEM., WAYNE STATE UNIV., DETROIT, MICH. 48202.
 SOURCE: J. Am. Chem. Soc., (1989) 111 (11), 4125-4126.
 CODEN: JACSAT. ISSN: 0002-7863.
 FILE SEGMENT: BR; OLD
 LANGUAGE: English

L6 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1984:434312 CAPLUS
 DOCUMENT NUMBER: 101:34312
 TITLE: Toxicological features of T 2 toxin and related trichothecenes
 AUTHOR(S): Ueno, Yoshio
 CORPORATE SOURCE: Fac. Pharm. Sci., Tokyo Univ. Sci., Tokyo, 162, Japan
 SOURCE: Fundamental and Applied Toxicology (1984), 4(2, Pt. 2), 124-32
 CODEN: FAATDF; ISSN: 0272-0590
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Toxicol. characteristics of toxin T 2 (I) [21259-20-1] and related trichothecenes, mycotoxins produced by *Fusarium*, *Trichoderma*, *Verrucaria*, and others, were investigated in regard to LD50 values, dermal toxicity, hematomol. changes, and tumorigenicity. The LD50 values (mg/kg) of I in adult male mice were orally 10.5, i.p. 5.2, s.c. 2.1, and i.v. 4.2, and those of nivalenol [23282-20-4] were i.p. 4.1 and i.v. 6.3.
 The lethal toxicity of I and nivalenol was approx. 10 times higher than deoxynivalenol [51481-10-8]. Newborn and immature animals were much more susceptible than adults. Inhalation expts. revealed that 33 ppb I for 160-min and 140 ppb for 30-min exposure were enough to cause death in mice within several days. The dermal toxicity of I and macrocyclic trichothecenes (verrucarin A [3148-09-2] and roridin A [14729-29-4]) was significantly higher than the other trichothecenes, and the induction of edema and other dermal toxicities is caused by direct attack of the trichothecenes on the capillary vessels. No tumorigenicity of fusarenon X [23255-69-8] to dermal tissues was shown in mice.

L6 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1980:70705 CAPLUS
 DOCUMENT NUMBER: 92:70705
 TITLE: Detection of *Fusarium* toxic strains
 AUTHOR(S): Payen, J.; Lafont, P.; Parache, R. M.; Boller, F.
 CORPORATE SOURCE: Lab. Mycol. Appl., ENSAIA, Nancy, F-54000, Fr.
 SOURCE: Collection de Medecine Legale et de Toxicologie Medicale (1978), Volume Date 1977, 107(Mycotoxines), 111-17
 CODEN: CMLMDW; ISSN: 0398-9119
 DOCUMENT TYPE: Journal
 LANGUAGE: French
 AB Human and mouse tumor cultures were incubated in terasaki plates with toxin T 2 (I) [21259-20-1], diacetoxyscirpenol (II) [2270-40-8], neopolanol (III) [36519-23-2], and butenolide [497-23-4] with a view to detg. the toxicity threshold (crit. titer). At the crit. level the toxins gave an asynchronous cell fraction, consisting of rounded granular cells which detached themselves and a fraction of fuse-shaped cells altered in situ. Sensitivity thresholds were for I 10, II 32, III 800, and butenolide 1800 .mu.g/g, resp., in the human cancer test cultures. Resp. values for the mouse cancer cultures were 64, 320, 800, and 20,000 .mu.g/g. For test with germinating *Lepidium sativum* seed, the resp. values were 800, 10,000, 50,000, and 250,000 .mu.g/g. The toxins inhibited the radicle growth with great regularity. The rapidity of the *L. sativum* tests permits its use in routine checking of foods. The 3 tests gave satisfactory results with fractionated extra. from *Fusarium poae*, both with fractions which contained I, II, and III, and therefore were toxic for chicken embryos, and in tests with fractions free of I-III which were not toxic to chicken embryos but affected the cancer cell cultures and *L. sativum* germination.

L6 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1982:162967 CAPLUS
 DOCUMENT NUMBER: 96:162967
 TITLE: Structural modifications of anguidin and antitumor activities of its analogs
 AUTHOR(S): Kaneko, T.; Schmitz, H.; Essery, J. M.; Rose, W.; Howell, H. G.; O'Herron, F. A.; Nachfolger, S.; Huftalen, J.; Bradner, W. T.; et al.
 CORPORATE SOURCE: Bristol Lab., Div. Bristol-Myers Co., Syracuse, NY, 13201, USA
 SOURCE: Journal of Medicinal Chemistry (1982), 25(5), 579-89
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Approx. 60 derivs. of anguidin e.g., I (R = H, ClCH2CO2 tetrahydropyranyl; R1 = Ac, H, R2 = H, acyl), were prepd. for evaluation of antitumor activities. Positions 3,4,8,9,10, and 15 were modified, and the resultant derivs. were screened against P-388 leukemia. Introduction of the C3-oxo and C3,C8-oxo groups markedly improved the antileukemic activity, whereas epoxidn. of the C9-C10 double bond or oxidn. of the C15 position diminished its activity. Selected derivs. were further tested in the L1210, B16, Lewis lung, Colon 36, and Colon 38 tumor lines. Among these compds. 4.beta.,15-diacetoxyscirpene-3,8-dione and 4.beta.-(chloroacetoxy)-15-acetoxyscirpene-3,8-dione were most active in various tumors.

L6 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1973:543406 CAPLUS
 DOCUMENT NUMBER: 79:143406
 TITLE: Comparative toxicology of trichothec mycotoxins. Inhibition of protein synthesis in animal cells
 AUTHOR(S): Ueno, Yoshio; Nakajima, Michiko; Sakai, Kosei; Ishii, Kenji; Sato, Norio; Shimada, Noriko
 CORPORATE SOURCE: Fac. Pharm. Sci., Sci. Univ. Tokyo, Tokyo, Japan
 SOURCE: Journal of Biochemistry (Tokyo, Japan) (1973), 74(2), 285-96
 CODEN: JOBIAO; ISSN: 0021-924X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Among 14 kinds of 12,13-epoxy-trichothec mycotoxins and related antibiotics tested, 12 inhibited the uptake of 14C-labeled leucine by whole cell rabbit reticulocytes. The mycotoxins inhibited the uptake of leucine and thymidine without affecting uracil uptake in Ehrlich ascite tumor cells. Rabbit reticulocyte polyribosomes were degraded by low trichothecene concns. In concns. lower than the inhibitory concns. of puromycin and cycloheximide, the trichothecenes inhibited poly-U-dependent synthesis of polyphenylalanine in cell-free reticulocyte and rat liver systems. Fusarenon-X [23255-69-8] did not inhibit protein synthesis in whole-cell or cell-free *Escherichia coli* systems, but slightly inhibited the uptake of it amino acids in yeast (*Geotrichum candidum*). Biochem. features of trichothec mycotoxin action are discussed in relation to their chem. and toxicol. characteristics.

L6 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1972:94528 CAPLUS
DOCUMENT NUMBER: 76:94528
TITLE: Cytotoxicity of sesquiterpene lactones
AUTHOR(S): Lee, Kuo-Hsiung; Huang, Eng-Shang; Piantadosi, Claude;
Pagano, Joseph S.; Geissman, T. A.
CORPORATE SOURCE: Dep. Med. Chem., Univ. North Carolina, Chapel Hill, NC, USA
SOURCE: Cancer Research (1971), 31(11), 1649-54
CODEN: CNREAS; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The toxicity of sesquiterpene lactones to 3 human cell lines is mainly due to an .alpha.-methylene-.gamma.-lactone moiety in the sesquiterpene molecules such as canin (I) [24959-84-0]. The cytotoxicity tests were performed in a microtest plate in which different concns. of 18 sesquiterpene lactones were simultaneously tested against 3 cell lines: human laryngeal carcinoma, normal human fibroblasts, and human cells transformed with simian virus 40. Hydrogenation of the conjugated .alpha.-methylene-.gamma.-lactone systems, as in .alpha.-santonin [481-06-1], vulgarin [3162-56-9], and desacetoxyatricarin [10180-88-8] led to essentially inactive compds., whereas the remaining sesquiterpene lactones contg. the O=C-C=CH2 system inhibited the growth of these cells.